

REMARKS

This application pertains to novel solid lipid particles of bioactive agents and methods for the manufacture and use thereof.

Claims 1-40, 42, 44 and 45 are pending, while Claims 1-15 and 37-39 have been withdrawn from consideration as drawn to non-elected subject-matter.

The Claims under consideration are Claims 16 - 36, 40, 42, 44 and 45.

It is respectfully requested that upon allowance of claims drawn to elected subject matter the non-elected claims be rejoined.

The claims have been amended to more specifically recite that the active substance (A) is initially in a crystalline form, but that it is suspended in a liquid, melted to form an emulsion and then immediately cooled to solidify the active ingredient amorphously. Further, the amorphous particles of the active ingredient are immediately coated with coating material (E) to prevent recrystallization. Applicants' process therefore provides a pulverulent active substance wherein the active substance, which was initially in crystalline form, is available in amorphous form.

It is totally surprising that the active ingredient (A), which was initially in crystalline form, remains in amorphous form and does not recrystallize (paragraph

[0032]). As a result of this, the bioavailability of the active ingredient remains very high (paragraph [0033]).

Those skilled in the art understand that an amorphous formulated drug is resorbed by the human body much faster than the same drug if in a crystalline state. Thus, Applicants' invention represents a tremendous advance in the state of the art!

Claims 16-36, 40, 42, 44 and 45 stand rejected under 35 U.S.C. 103(a) as obvious over Irvin (US 7,276,184) in view of Westesen et al. (US 5,885,486) and further in view of Jordan et al. (US 2002/0103285).

Contrary to Applicants' invention, Irvin produces particles of bioactive agents which are in the crystalline form ! See, for example:

Col. 1, line 26,

Col. 5, line 16,

Col. 11, line 39,

Col. 11, line 47,

Col. 12, line 32,

Col. 16, line 10,

Col. 17, line 12m

Col. 17, line 23, and

Col. 19, line 66.

Furthermore, Irvin specifically **teaches away** from Applicants' invention where, at Col. 5, line 29, he teaches that his particles are..."not in an amorphous..." form.

No person reading Irving could possibly ever be led to a process wherein an active ingredient, originally in crystalline form, can be prepared as amorphous particles which are prevented from recrystallizing.

The Examiner relies on Westesen for a freeze drying process (page 5, second paragraph, of the office action). No freeze drying process could ever overcome the differences between Applicants' process for producing particles having an active ingredient in amorphous form and Irvin's process for producing particles of an active ingredient in crystalline form.

In this regard, it is noted that the Examiner, at page 5 of the office action, refers specifically to Westesen's Example 19. The Examiner's attention is respectfully drawn to lines 52 and 53 of Westesen's Example 19, where Westesen's teaches that the product of his Example 19 is **recrystallized** !

Clearly, no combination of Irvin and Westesen could possibly lead to a process wherein an active ingredient, originally in crystalline form, can be prepared as amorphous particles which are prevented from recrystallizing.

The Examiner relies on the Jordan reference for a dry film coating of polyvinyl alcohol. Nothing in this reference teaches or suggests that a polyvinyl alcohol coating

should be applied to a particle of an active ingredient, which is normally in crystalline form but which has been transformed into amorphous form, before it could recrystallize and thereby prevent it from recrystallizing. Nothing in Jordan suggests that the tablets e.g. of Jordan's Example 1 were a type that was in amorphous form, but which would recrystallize to a crystalline form and that the coating was applied before recrystallization took place and prevented such recrystallization. Moreover, as discussed above, the Irvin/Westesen combination of references pertain to an active ingredient in **crystalline** (not amorphous) form. If one were to coat the Irvin/Westesen particles with Jordan's dry film coating, one would end-up with a particle in crystalline form, coated with the dry coating.

No combination of Irvin/Westesen/Jordan could ever lead those skilled in the art to a process wherein an active ingredient, normally in crystalline form, is suspended in an aqueous phase, melted, then cooled to solidify amorphously and prevented from recrystallizing by a coating of a substance such as polyvinyl alcohol.

Accordingly, Applicants' claims cannot be seen as obvious over any combination of Irvin, Westesen, and Jordan and the rejection of claims 16-36, 40, 42, 44 and 45 under 35 U.S.C. 103(a) as obvious over Irvin (US 7,276,184) in view of Westesen et al. (US 5,885,486) and further in view of Jordan et al. (US 2002/0103285) should now be withdrawn.

Finally, claim 42 stands rejected under 35 U.S.C. 103(a) as obvious over Irvin (US 7,276,184) in view of Westesen et al. (US 5,885,486), Jordan et al. (US 2002/0103285) and further in view of Rochling et al. (US 6,602,823).

The differences between Applicants' invention and anything that could be learned from the of Irvin/ Westesen/Jordan combination of references are discussed above. The Examiner relies on Rochling for specific additives. None of the additives taught by Rochling could possibly overcome the differences discussed above, however, and the rejection of claim 42 under 35 U.S.C. 103(a) as obvious over Irvin (US 7,276,184) in view of Westesen et al. (US 5,885,486), Jordan et al. (US 2002/0103285) and further in view of Rochling et al. (US 6,602,823) should now be withdrawn.

In view of the present amendments and remarks it is believed that claims 1-40, 42, 44 and 45 are now in condition for allowance. Reconsideration of said claims by the Examiner is respectfully requested and the allowance thereof is courteously solicited. Should the Examiner not deem the present amendment and remarks to place the instant claims in condition for allowance, it is respectfully requested that this Amendment Under Rule 116 be entered for the purpose of placing the prosecution record in better condition for appeal.

CONDITIONAL PETITION FOR EXTENSION OF TIME

If any extension of time for this response is required, Appellants request that this be considered a petition therefor. Please charge the required petition fee to Deposit Account No. 14-1263.

ADDITIONAL FEE

Please charge any insufficiency of fee or credit any excess to Deposit Account No. 14-1263.

Respectfully submitted,
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